FORM PTO-1390 (REV. 11-94)

U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER 8265-269

09/355363

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US)

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP98/00522	January 21, 1998	February 28, 1997

TITLE OF INVENTION
MODIFYING AND SUPPLYING LIQUID NUTRITIONAL FEEDING

APPLICANT(S) FOR DO/EO/US
BOURGUIGNON, Michel

Applicant herewith submits to the United States Designated/ Elected Office (DO/EO/US) the following items under 35 U.S.C. 371:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.

2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.

3. ☒ This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).

4. ☒ A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.

5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☒ is transmitted herewith (required only if not transmitted by the international Bureau).
   b. ☐ has been transmitted by the International Bureau (PCT Rule 47.1(c) Notice Enclosed).
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US)

6. ☐ A translation of the International Application into English (35 U.S.C. 371(c)(2)) with Certificate of Verification.

7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are transmitted herewith (required only if not transmitted by the International Bureau).
   b. ☐ have been transmitted by the International Bureaus.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☒ have not been made and will not be made.

8. ☐ A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 37(c)(3)).

9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).

10. ☒ The International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98 with copies of the references.

12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.

13. ☒ A FIRST preliminary amendment.
    ☐ A SECOND or SUBSEQUENT preliminary amendment.

14. ☒ A substitute specification.

15. ☐ A change of power of attorney and/or address letter.

16. ☒ Other items or information:
    1) International Search Report
    2) Formal Drawings

INTERNATIONAL APPLICATION NO PCT/EP98/00522 09/355363 | INTERNATIONAL FILING DATE January 21, 1998 | Rec'd PCT/PTO 28 JUL 1999

17. ☒ The U.S. National Fee (35 U.S.C. 371(c)(1)) and other fees as follows:

	CLAIMS			
(1)FOR	(2)NUMBER FILED	(3)NUMBER EXTRA	(4)RATE	(5)CALCULATIONS
TOTAL CLAIMS	12 - 20	0	X $ 18.00	$ 0.00
INDEPENDENT CLAIMS	1 - 3	0	X $ 78.00	0.00
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $ 260.00	☐
BASIC NATIONAL FEE (37 CFR 1.492(a)(1)-(5)): **CHECK ONE BOX ONLY**				
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) ..... $ 670				
☐ No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) ..... $ 760				
☒ Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO $970				$ 970.00
☐ International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(2) to (4) ..... $ 96				$
☐ Filing with EPO or JPO search report ..... $ 840				
Surcharge of $130.00 for furnishing the National fee or oath or declaration later than 20 30 mos. from the earliest claimed priority date (37 CFR 1.492(e)).				
		TOTAL OF ABOVE CALCULATIONS	=	970.00
Reduction by 1/2 for filing by small entity, if applicable. Affidavit must be filed also. (Note 37 CFR 1.9, 1.27, 1.28).			-	$ 0.00
		SUBTOTAL	=	970.00
Processing fee of $130.00 for furnishing the English Translation later than 20 30 mos. from the earliest claimed priority date (37 CFR 1.492(f)).			+	
0		TOTAL FEES ENCLOSED		$ 970.00

a. ☐ A check in the amount of $__ to cover the above fees is enclosed.

b. ☒ Please charge Deposit Account No. 16-1150 in the amount of $970.00 to cover the above fees. A copy of this sheet is enclosed.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 16-1150. A copy of this sheet is enclosed.

18. ☐ Other instructions

n/a

19. ☒ All correspondence for this application should be mailed to

PENNIE & EDMONDS LLP
1667 K STREET, N.W.
WASHINGTON, D.C. 20006

20. ☒ All telephone inquiries should be made to (202) 496-4720

Allan A. Fanucci	Allan A. Fanucci	30,256	7/28/99
NAME	SIGNATURE	REGISTRATION NUMBER	DATE

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Michel BOURGUIGNON

Application No.: To Be Assigned (National Stage of PCT/EP98/00522)	Group Art Unit: To Be Assigned
Filed: Concurrently herewith	Examiner: To Be Assigned
For: MODIFYING AND SUPPLYING NUTRITIONAL FEEDING	Attorney Docket No.: 8265-269

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please enter the following amendments and remarks into the file of the above-identified application prior to the examination thereof.

IN THE SPECIFICATION

Please amend the specification as follows. A marked-up version of the specification, in English, is attached hereto with amendments noted in red ink. In addition, a substitute specification which includes these amendments is also attached.

Page 1, between the title and the first line of text, insert: --TECHNICAL FIELD--;

Page 1, line 8: insert --BACKGROUND--;

Page 1, line 15: change "the variation of" to --varying--;

Page 1, line 16: change "for" to --to--;

Page 1, line 17: change "a tailoring of " to --tailor--;

Page 1, line 25: change "increase" to --decrease--;

Page 2, line 10: change "passing" to --passed--;

Page 2, line 11: change "to" to "before entering";

Page 2, line 14: change "is passing" to --passes--;

Page 2, line 22: after "example" insert --,-- and delete the first occurrence of "the";

Page 3, before line 1: insert --SUMMARY OF THE INVENTION--;

Page 3, line 4: after "delivery" insert --apparatus--, and change "for the" to --with a--;

Page 3, line 10: after "agent" insert --by--;

Page 4, line 3: change "to" to --and--;

Page 4, line 23: change "the" to --a--;

Page 4, line 24: change "the" to --has– and delete "of";

Page 5, line 13: after "it" insert --may--, and change "comprises" to --comprise--;

Page 5, line 23: change the second occurrence of "the" to --an--;

Page 6, line 1: delete "an";

Page 6, line 5: change "of" to --from--;

Page 6, line 15: after "is/are" insert --, for– and after "e.g." insert --,--;

Page 6, line 20: delete "or each", change "agent" to --agent(s)--, and after "is" insert --/are--;

Page 7, line 13: change "and" to --,--, and after "antioxidants" insert --,--;

Page 8, line 5: insert --BRIEF DESCRIPTION OF THE DRAWINGS--;

Page 8, line 16: insert --DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS--;

Page 9, line 2: delete "the";

Page 9, line 11: after "plastic" insert --, for--, after "e.g." insert --,-- and change "Polycinyl" to --Polyvinyl--;

Page 9, line 12: after "plastic" insert --, for--, after "e.g." insert --,-- and change "Polycinyl" to --Polyvinyl--;

Page 9, line 14: after "may" insert --, for--, and after "e.g." insert --,--;

Page 9, line 16: after "threads" insert --4--, and delete --4--;

Page 10, line 14: after "are" insert --,--, after "example" insert --,--, after "out" insert --by--, and after "following" insert --:--;

Page 11, line 9: change "is" to --as--;

Page 11, line 13: change "e.g." to --for--;

Page 11, line 18: change "a" to --this--;

Page 11, line 29: change "A" to "The";

Page 12, line 15: delete "a" and change the second occurrence of "in" to --of--;

Page 12, line 16: change "composition," to --compositions--;

Page 12, line 17: change "homogeneously." to --homogeneous at--;

Page 12, line 24: change "are" to --were--;

Page 13, before claim 1, insert --What is claimed is:--.

IN THE CLAIMS

Please cancel claims 10 and 11 and amend the claims as follows:

1. (Amended) An apparatus for modifying and feeding a liquid nutritional feeding composition comprising,

a chamber for receiving at least one [a] beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container that contains [containing] the nutritional feeding composition and an outlet connectable to a feeding means, and

a pumping means associated with the chamber for pumping the [said] nutritional feeding composition from the container into the chamber and back into [to] the container to mix [for mixing] the beneficial agent and [into] the nutritional feeding composition.

2. (Amended) An apparatus according to claim 1, wherein the [volume of the chamber being alterable for] pumping means comprises [of the nutritional feeding composition] varying the volume of the chamber.

3. (Amended) An apparatus according to [either] claim [1 or] 2, wherein the chamber comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition.

4. (Amended) An apparatus according to [any of claims] claim 1 [to 3], wherein the chamber comprises at least one beneficial agent selected from the group

consisting of nutrients, probiotics, medicaments, [(and] diagnostic agents[)], [or a (physiological) combination] and mixtures thereof.

5. (Amended) An apparatus according to [any of claims] claim 1 [to 4], wherein the at least one [or each] beneficial agent is dispersible in the nutritional feeding composition in less than 1 min.

6. (Amended) An apparatus according to [any of claims] claim 1 [to 4], wherein the at least one [or each] beneficial agent is dispersible in the nutritional feeding composition in less than 30 sec.

7. (Amended) An apparatus according to [any of claims] claim 4 [to 6], wherein the volume of beneficial agent constitutes from 30% to 50% of the volume of the chamber.

8. (Amended) An apparatus according to [any of claims] claim 1 [to 7], wherein the inlet is provided with a hollow spike for piercing [of] a port on [of] the container to create [and creating] a fluid path for the nutritional feeding composition.

9. (Amended) An apparatus according to [any of claims] claim 1 [to 8], wherein the feeding means comprises a hollow spike for piercing the outlet of the chamber to create [and creating] a fluid path for the nutritional feeding composition with the beneficial agent.

12. (Amended) A method for modifying and feeding a liquid nutritional feeding composition comprising:[,]

connecting a chamber according to [any of claims] claim 1 [to 2] to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber and liquid nutritional feeding composition and beneficial agent back to the container to mix the nutritional feeding composition with the beneficial agent,

connecting the feeding means to the outlet of the chamber [according to either claims 1 or 9], and

allowing the modified nutritional feeding composition to flow through the chamber into the feeding means.

Please add the following new claims:

13. (New) The method of claim 12 wherein the feeding involves enterally supplying the liquid nutritional feeding composition.

14. (New) The method of claim 12 wherein the feeding involves intravenously supplying the liquid nutritional feeding composition.

IN THE ABSTRACT

Delete the abstract and substitute the following therefor:

--The present invention relates to an apparatus for modifying and feeding a liquid nutritional feeding composition. The apparatus comprises a chamber (3) for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber has an inlet (7) connectable to a container (5) that contains the nutritional feeding composition and an outlet (13) connectable to a feeding means (8,9). A pumping means is associated with the chamber (3) for pumping the nutritional feeding composition from the container into the chamber and back into the container to mix the beneficial agent with the nutritional feeding composition before the outlet (13) of the chamber is connected to the feeding means (8,9). The chamber (3) may comprise at least one flexible wall capable of being squeezed and released for pumping the nutritional feeding composition. The invention also relates to a method for modifying and feeding a liquid nutritional feeding composition.--

REMARKS

Applicants have amended the specification and claims to correct syntactic errors and improve clarity, to conform with U.S. patent practice, and to more clearly define the scope of protection sought by the present application.

No fee is believed to be due for entry of this Preliminary Amendment. However, if any fee should be required, please charge such fee to Pennie & Edmonds LLP Deposit Account No. 16-1150.

Date 7/28/99

Respectfully submitted,

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MODIFYING AND SUPPLYING LIQUID NUTRITIONAL FEEDING

TECHNICAL FIELD

The present invention relates to an apparatus and method for modifying and feeding a liquid nutritional feeding composition, in particular to its modification by adding a beneficial agent to the liquid feeding composition, before feeding said liquid feeding composition.

BACKGROUND

It is known to enterally or intravenously feed liquid nutrition to patients who are not able to eat by themselves. Such liquid meals are normally provided in hangable containers such as bottles or plastic bags and are fed from the containers through a tube to the patient. A number of different liquid nutritional feeds are available for ~~the variation~~ varying of the nutritional intake of the patient. Nevertheless, there is a need ~~for a tailoring of~~ to tailor the liquid meals to the patient's individual needs. This is known to be done by adding beneficial agents such as for example nutrients, probiotics and medicaments to the liquid nutritional feed. The adding of such beneficial agents should, for some applications, preferably take place just before the feeding starts as a premature mixing of the liquid nutritional feed and the beneficial agent may considerably ~~increase~~ decrease the quality and shelf-life of the liquid nutritional feed.

The liquid meals provided in hangable containers such as bottles or plastic bags are generally aseptically processed or terminally retorted before use. This

increases the shelf life of the liquid meal. For providing an aseptic feed to the patient, the container is connected directly via a feeding tube or line to the patient. Any opening of the system for adding a beneficial agent increases the risk for bacterial growth or contamination. A closed-line system for the modifying and feeding of patients is therefore desirable.

The prior art discloses closed-line systems wherein a liquid nutritional feeding composition is ~~passing~~ passed through a chamber comprising a beneficial agent ~~to~~ before entering the patient feeding line. The beneficial agent is mixed or dissolved in the liquid nutritional feeding composition when it ~~is passing~~ passes through the chamber.

In order to homogenise the feed to the patient in this type of feeding system and thus prevent an over concentration of the beneficial agent, it is necessary to control the release of the beneficial agent. Consequently, a beneficial agent in controlled release form is used, i.e. an agent the solubility of which is delayed or retarded. For example, ~~the~~ supplying of the liquid nutritional feed releases the beneficial agent over a period of 2 to 24 hours. Furthermore, although the controlled release form allows the beneficial agent to be released over a period, in-homogeneity may be experienced in the start-up phase due to the protective coating on the beneficial agents.

Summary of the Invention

It is an object of the invention to provide an improved system for modifying and feeding a homogeneous mixture of a liquid nutritional feed and a beneficial agent. In particular to provide a delivery apparatus useable with a ~~for the~~ beneficial agent in a non-controlled release form.

It is a further object of the invention to provide a closed-line system for modifying and feeding a mixture of a liquid nutritional feed composition and a beneficial agent by allowing the operations to take place without opening the system to bacteria or contamination.

Accordingly, in a first aspect, the invention concerns an apparatus for modifying and feeding a liquid nutritional feeding composition comprising,

a chamber for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container containing the nutritional feeding composition and an outlet connectable to a feeding means, and

a pumping means associated with the chamber for pumping the nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition.

Thus, the present invention provides an apparatus for modifying and feeding a liquid nutritional feeding composition which allows the addition of a beneficial agent to the liquid feed immediately before the feeding

commences, which addition of the beneficial agent is done without an opening and reclosing of the system. The mixing of the beneficial agent ~~to~~ and the liquid feeding is conducted by pumping means arranged to pump liquid feed from the container into the chamber and liquid and beneficial agent back into the container. After end mixing, the chamber is connected to feeding means for feeding of the mixture to the patient.

It has been found that a homogeneous modification and feeding can be obtained with the feeding system according to the invention. Furthermore, it has been found that the mixture of liquid feed and the beneficial agent is stable during 48 hours' feeding.

In a particularly advantageous embodiment of the invention the pumping means is adapted to vary the volume of the chamber being used for pumping of the nutritional feeding composition. Especially preferred is an embodiment of the invention wherein the chamber comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition. For example, ~~the~~ a wall of plastic material ~~the~~ has flexibility ~~of~~ which allows a deformation of the wall.

For the embodiment of the above-mentioned flexible wall type, in order to obtain an appropriate pumping effect and thus limit the number of pumping cycles necessary for the mixing of the beneficial agent with the liquid,

the chamber should not be too full of the beneficial agent. Conveniently, at least 30% of the volume of the chamber is empty in the un-squeezed state. Preferably, the volume of beneficial agent constitutes from 5% to 70%, preferably from 30% to 50% of the volume of the chamber. The limits of the ratio filled and un-filled volume will depend on the solubility of the product.

The liquid nutritional feeding composition is of a conventional type. The liquid nutritional feeding composition may comprise from 0 to 25% protein, from 0 to 50% lipids, and from 0 to 60% carbohydrates. For example, it may comprise about 15% protein, about 35% lipids, and about 50% carbohydrates. The water content is preferably from 70 to 95% by weight.

The chamber may be delivered as a sealed unit comprising the beneficial agent. Alternatively, the chamber may be filled with the beneficial agent at the location where the treatment is to take place.

The connections between the container, the chamber, and the feeding means are preferably as follows: ~~the~~ an inlet is provided with a hollow spike for piercing of a port of the container and creating a fluid path for the nutritional feeding composition. The feeding means comprises a hollow spike for piercing the outlet of the chamber and creating a fluid path for the nutritional feeding composition with the beneficial agent. The piercing of the outlet of the chamber is done after end

mixing. The present system of connection allows for ~~an~~ on-line feeding of an aseptic liquid nutritional feeding composition with a beneficial agent.

The flow ~~of~~ from the container to and through the feeding tube means may be due to gravity alone, but preferably the flow from the container to and through the feeding tube means is assisted by a pump.

The beneficial agent is dispersible in the nutritional liquid feed. By dispersible is understood, soluble as well as agents that are suspendable so as to be mixed with the liquid feed and forwarded herewith.

The beneficial agent or agents is/are, for e.g., selected from the group consisting of nutrients, probiotics, medicaments and diagnostic tracer or a physiological combination thereof.

It is preferred that the ~~or each~~ beneficial agent(s) is/are dispersible in the nutritional feeding composition in less than 1 min, more preferably in less than 30 sec.

For beneficial agents that are stable in liquid conditions, the agents may be provided in liquid form. Even if the beneficial agent is stable in a certain liquid formulation, a mixture of the liquid nutritional feeding composition and the liquid beneficial agent may not be stable for a longer period, thus the apparatus according to the invention may advantageously be used.

For enteral feeding the beneficial agents are cleaned but there is no need for a sterile product. However, for intravenously fed liquid, the beneficial agent must be sterilised.

The beneficial agent preferably comprises nutrients selected from the group consisting of glutamine, vitamins, arginine, fermentable and non-fermentable dietary fibres, enzymes, oligo elements, combinations of amino acids, oligosaccharides, short chain fatty acids, salts, structured lipids, d-cyroinositol, lactoferrin, marine oils, ~~and~~ acidulents, antioxidants, or a combination thereof.

The apparatus according to the invention may advantageously be used for enteral or intravenous feeding. For intravenous feeding the beneficial agent is sterilised.

In a second aspect, the invention relates to a method for modifying and feeding a liquid nutritional feeding composition comprising,

connecting a chamber, of the kind described above, to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber, and liquid nutritional feeding composition and the beneficial agent back to the container to mix with the nutritional feeding composition,

connecting the feeding means, and

allowing the modified nutritional feeding composition to flow through the chamber into the feeding means.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further detail by way of examples only with reference to the accompanying drawings and examples, in which

Fig. 1 is a principle drawing illustrating enteral feeding of a patient with an apparatus according to the invention,

Fig.2 is a cross-sectional principle drawing of the chamber for receiving a beneficial agent, and

Fig. 3 shows a measure of levels of beneficial agent in a feed.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Fig. 1 shows an apparatus 1 according to the invention arranged for modifying and feeding a liquid nutritional feed 6 to a patient, not shown in the drawings. The apparatus 1 comprises a chamber 3 containing a beneficial agent. The chamber 3 is connected to a container 5 containing the nutritional feeding composition 6 via an inlet 7. An outlet 13 in the chamber 3 is connected to feeding tubes 8 and 9 which serve to lead the modified feeding composition to the patient. The feeding tube 9 extends through the nasal path and to the stomach of the patient. Pumping means is provided in the form of the chamber 3 which has a flexible wall structure 12 for pumping the liquid feeding composition 6 into the chamber 3 and back to the

container 5 so as to modify the liquid feeding composition 6. In order to assure attachment between ~~the~~ parts 5, 7, 8, 9 and 13, conventional fastening means 17 and 18 are provided. Furthermore, a pump 10 to assist the flow from the outlet 13 and flow regulation means 11 are provided.

Fig. 2 illustrates a chamber 3 according to the invention. The chamber 3 comprises an inlet 7 and an outlet 13. A chamber wall 12 is provided in a flexible plastic, for e.g., soft ~~Polycinyl~~ Polyvinyl Chloride and a rigid lid 14 is made from a harder plastic, for e.g., hard ~~Polycinyl~~ Polyvinyl Chloride. In the present embodiment the inlet 7 is defined in the lid 14. The lid 14 may, for e.g., be sealed onto the wall 12 by ultrasonic welding or provided with threads, 4 and screwed ~~4~~ onto the wall 12.

Before use, the chamber 3 the inlet 7 and the outlet 13 are closed by thin membranes 15 and 16. For the initial mixing of a beneficial agent with a liquid feeding composition, the inlet's membrane 15 is first pierced when being connected to the container 5 shown in Fig. 1. Upon end pumping and mixing, the tube feeding 8 of Fig. 1 is to be connected to the chamber 3 which results in a piercing of the outlet's membrane 16.

EXAMPLE 1

Several liquid nutritional feeding compositions are modified and fed by

1) connecting containers of liquid, feeding to a flexible chamber according to the invention, by piercing the port in the container with the spike of the container,

2) pumping liquid from the container to the chamber and back again by squeezing and releasing the chamber 3 to 5 times, and

3) connecting the feeding means by piercing the outlet of the chamber, thus feeding the modified liquid feed composition to the feeding means. The flow is by gravity or assisted by a pump.

Tests are, for example, carried out by feeding:

1) 12 g glutamine as beneficial agent constituting about 60% of the volume of the chamber with 500 ml or 1 L liquid feed.

2) 1 g pro-biotic as beneficial agent constituting about 5% of the volume of the chamber with 500 ml or 1 L liquid feed.

3) 12 g glutamine mixed with 1 g pro-biotic as beneficial agent constituting in total about 65% of the volume of the chamber with 500 ml or 1 L liquid feed.

The liquid feeds are commercially available products such as Réabilan HN, Réabilan, Sondalis ISO, and Sondalis HP supplied by Nestlé S.A. Switzerland.

The modified feed is inspected and characterised as homogeneous.

EXAMPLE 2 - Stability

The stability of the mixture of the liquid nutritional feeding composition and the beneficial agent are controlled by the level of beneficial agent ~~is~~ as measured by means of a calorimetric method (Kit Boehringer).

Mixtures of liquid nutritional feeding composition and beneficial agent are fed and samples are stored ~~e.g.~~ for 24 hours and 48 hours and the level of beneficial agent is measured.

For example, the stability of Sondalis ISO and Réabilan HN comprising Glutamine are measured over ~~a~~ this period:

	Sondalis ISO	Réabilan HN
T= 0h	12,9 g/l	14,6 g/l
T= 24h	12.6 g/l	13,5 g/l
T= 48h	12.5 g/l	12,9 g/l

The measurements show that the Glutamine is stable above a level of 12 g/l after 48 hours.

EXAMPLE 3 - Homogenisation

~~A~~ The homogeneity of the modified liquid nutritional feeding composition is controlled by mixing the beneficial agent

or agents with the liquid nutritional feeding composition by pumping 5 times the liquid into and out of the chamber.

The feeding tube or line is connected to the chamber and an enteral pump running at 100 ml/h, corresponding to a continuous nutrition (24h/42h).

During the feeding, after each 50 ml fed, the level of beneficial agent is measured by means of a calorimetric method (Kit Boehringer).

Fig. 3 shows the amount of beneficial agent in a feed, in the example in question the beneficial agent is Glutamine in ~~a~~ 500 ml ~~in~~ of 4 different liquid feeding compositions. It is apparent from the figure that the Glutamine level is ~~homogeneously~~ homogeneous at about 12-14 g/l during the feeding period.

EXAMPLE 4

In order to verify that the geometry of the liquid containing container did not influence the homogenisation of the modified feed, trials ~~are~~ were conducted with drip-pack, plastic pouches, and glass bottles. No difference in the homogeneity was detected from the various containers.

CLAIMS

What is claimed is:

1. An apparatus for modifying and feeding a liquid nutritional feeding composition comprising,

a chamber for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container containing the nutritional feeding composition and an outlet connectable to a feeding means, and

a pumping means associated with the chamber for pumping said nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition.

2. An apparatus according to claim 1, wherein the volume of the chamber being alterable for pumping of the nutritional feeding composition.

3. An apparatus according to either claim 1 or 2, wherein the chamber comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition.

4. An apparatus according to any of claims 1 to 3, wherein the chamber comprises at least one beneficial agent selected from the group consisting of nutrients, probiotics, medicaments (and diagnostic agents) or a (physiological) combination thereof.

5. An apparatus according to any of claims 1 to 4, wherein the or each beneficial agent is dispersible in the nutritional feeding composition in less than 1 min.

6. An apparatus according to any of claims 1 to 4, wherein the or each beneficial agent is dispersible in the nutritional feeding composition in less than 30 sec.

7. An apparatus according to any of claims 4 to 6, wherein the volume of beneficial agent constitutes from 30% to 50% of the volume of the chamber.

8. An apparatus according to any of claims 1 to 7, wherein the inlet is provided with a hollow spike for piercing of a port of the container and creating a fluid path for the nutritional feeding composition.

9. An apparatus according to any of claims 1 to 8, wherein the feeding means comprises a hollow spike for piercing the outlet of the chamber and creating a fluid path for the nutritional feeding composition with the beneficial agent.

10. Use of an apparatus according to any of claims 1 to 9 for modifying and enterally supplying of liquid nutritional feeding composition.

11. Use of an apparatus according to any of claims 1 to 9 for modifying and intravenous supplying of liquid nutritional feeding composition.

12. A method for modifying and feeding a liquid nutritional feeding composition comprising,

connecting a chamber according to any of claims 1 to 2 to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber and liquid nutritional feeding composition and beneficial agent back to the container to mix the nutritional feeding composition,

connecting the feeding means according to either claims 1 or 9, and

allowing the modified nutritional feeding composition to flow through the chamber into the feeding means.

13. A method according to claim 12, wherein the flow from the container to and through the feeding tube means, is due to gravity.

14. A method according to claim 12, wherein the flow from the container to and through the feeding tube means, is assisted by a pump.

ABSTRACT

The present invention relates to an apparatus for modifying and feeding a liquid nutritional feeding composition. Said apparatus comprises 1) chamber (5) for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet (7) connectable to a container (5) containing the nutritional feeding composition and an outlet (13) connectable to a feeding means (8,9) and a pumping means associated (3) with the chamber for pumping said nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition before connecting the outlet (13) of said chamber to the feeding means (8,9). It is preferred that the chamber (3) comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition. The invention also relates to a method for modifying and feeding a liquid nutritional feeding composition.

MODIFYING AND SUPPLYING LIQUID NUTRITIONAL FEEDING

TECHNICAL FIELD

The present invention relates to an apparatus and method for modifying and feeding a liquid nutritional feeding composition, in particular to its modification by adding a beneficial agent to the liquid feeding composition, before feeding said liquid feeding composition.

BACKGROUND

It is known to enterally or intravenously feed liquid nutrition to patients who are not able to eat by themselves. Such liquid meals are normally provided in hangable containers such as bottles or plastic bags and are fed from the containers through a tube to the patient. A number of different liquid nutritional feeds are available for varying the nutritional intake of the patient. Nevertheless, there is a need to tailor the liquid meals to the patient's individual needs. This is known to be done by adding beneficial agents such as for example nutrients, probiotics and medicaments to the liquid nutritional feed. The adding of such beneficial agents should, for some applications, preferably take place just before the feeding starts as a premature mixing of the liquid nutritional feed and the beneficial agent may considerably decrease the quality and shelf-life of the liquid nutritional feed.

The liquid meals provided in hangable containers such as bottles or plastic bags are generally aseptically processed or terminally retorted before use. This increases the shelf life of the liquid meal. For providing an aseptic feed to the patient, the container is connected directly via a feeding tube or line to the patient. Any opening of the system for adding a beneficial agent increases the risk for bacterial growth or contamination.

A closed-line system for the modifying and feeding of patients is therefore desirable.

The prior art discloses closed-line systems wherein a liquid nutritional feeding composition is passed through a chamber comprising a beneficial agent before entering the patient feeding line. The beneficial agent is mixed or dissolved in the liquid nutritional feeding composition when it passes through the chamber.

In order to homogenise the feed to the patient in this type of feeding system and thus prevent an over concentration of the beneficial agent, it is necessary to control the release of the beneficial agent. Consequently, a beneficial agent in controlled release form is used, i.e. an agent the solubility of which is delayed or retarded. For example, supplying of the liquid nutritional feed releases the beneficial agent over a period of 2 to 24 hours. Furthermore, although the controlled release form allows the beneficial agent to be released over a period, in-homogeneity may be experienced in the start-up phase due to the protective coating on the beneficial agents.

SUMMARY OF THE INVENTION

It is an object of the invention to provide an improved system for modifying and feeding a homogeneous mixture of a liquid nutritional feed and a beneficial agent. In particular to provide a delivery apparatus useable with a beneficial agent in a non-controlled release form.

It is a further object of the invention to provide a closed-line system for modifying and feeding a mixture of a liquid nutritional feed composition and a beneficial agent by allowing the operations to take place without opening the system to bacteria or contamination.

Accordingly, in a first aspect, the invention concerns an apparatus for modifying and feeding a liquid nutritional feeding composition comprising,

a chamber for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container containing the nutritional feeding composition and an outlet connectable to a feeding means, and

a pumping means associated with the chamber for pumping the nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition.

Thus, the present invention provides an apparatus for modifying and feeding a liquid nutritional feeding composition which allows the addition of a beneficial agent to the liquid feed immediately before the feeding commences, which addition of the beneficial agent is done without an opening and reclosing of the system. The mixing of the beneficial agent and the liquid feeding is conducted by pumping means arranged to pump liquid feed from the container into the chamber and liquid and beneficial agent back into the container. After end mixing, the chamber is connected to feeding means for feeding of the mixture to the patient.

It has been found that a homogeneous modification and feeding can be obtained with the feeding system according to the invention. Furthermore, it has been found that the mixture of liquid feed and the beneficial agent is stable during 48 hours' feeding.

In a particularly advantageous embodiment of the invention the pumping means is adapted to vary the volume of the chamber being used for pumping of the nutritional feeding composition. Especially preferred is an embodiment of the invention wherein the chamber comprises at least one flexible wall capable of being squeezed and released for

pumping of the nutritional feeding composition. For example, a wall of plastic material has flexibility which allows a deformation of the wall.

For the embodiment of the above-mentioned flexible wall type, in order to obtain an appropriate pumping effect and thus limit the number of pumping cycles necessary for the mixing of the beneficial agent with the liquid, the chamber should not be too full of the beneficial agent. Conveniently, at least 30% of the volume of the chamber is empty in the un-squeezed state. Preferably, the volume of beneficial agent constitutes from 5% to 70%, preferably from 30% to 50% of the volume of the chamber. The limits of the ratio filled and un-filled volume will depend on the solubility of the product.

The liquid nutritional feeding composition is of a conventional type. The liquid nutritional feeding composition may comprise from 0 to 25% protein, from 0 to 50% lipids, and from 0 to 60% carbohydrates. For example, it may comprise about 15% protein, about 35% lipids, and about 50% carbohydrates. The water content is preferably from 70 to 95% by weight.

The chamber may be delivered as a sealed unit comprising the beneficial agent. Alternatively, the chamber may be filled with the beneficial agent at the location where the treatment is to take place.

The connections between the container, the chamber, and the feeding means are preferably as follows: an inlet is provided with a hollow spike for piercing of a port of the container and creating a fluid path for the nutritional feeding composition. The feeding means comprises a hollow spike for piercing the outlet of the chamber and creating a fluid path for the nutritional feeding composition with the beneficial agent. The piercing of the outlet of the chamber is done after end mixing. The present system of

connection allows for on-line feeding of an aseptic liquid nutritional feeding composition with a beneficial agent.

The flow from the container to and through the feeding tube means may be due to gravity alone, but preferably the flow from the container to and through the feeding tube means is assisted by a pump.

The beneficial agent is dispersible in the nutritional liquid feed. By dispersible is understood, soluble as well as agents that are suspendable so as to be mixed with the liquid feed and forwarded herewith.

The beneficial agent or agents is/are, for e.g., selected from the group consisting of nutrients, probiotics, medicaments and diagnostic tracer or a physiological combination thereof.

It is preferred that the beneficial agent(s) is/are dispersible in the nutritional feeding composition in less than 1 min, more preferably in less than 30 sec.

For beneficial agents that are stable in liquid conditions, the agents may be provided in liquid form. Even if the beneficial agent is stable in a certain liquid formulation, a mixture of the liquid nutritional feeding composition and the liquid beneficial agent may not be stable for a longer period, thus the apparatus according to the invention may advantageously be used.

For enteral feeding the beneficial agents are cleaned but there is no need for a sterile product. However, for intravenously fed liquid, the beneficial agent must be sterilised.

The beneficial agent preferably comprises nutrients selected from the group consisting of glutamine, vitamins, arginine, fermentable and non-fermentable dietary fibres, enzymes, oligo elements, combinations of amino acids,

oligosaccharides, short chain fatty acids, salts, structured lipids, d-cyroinositol, lactoferrin, marine oils, acidulents, antioxidants, or a combination thereof.

The apparatus according to the invention may advantageously be used for enteral or intravenous feeding. For intravenous feeding the beneficial agent is sterilised.

In a second aspect, the invention relates to a method for modifying and feeding a liquid nutritional feeding composition comprising,

connecting a chamber, of the kind described above, to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber, and liquid nutritional feeding composition and the beneficial agent back to the container to mix with the nutritional feeding composition,

connecting the feeding means, and

allowing the modified nutritional feeding composition to flow through the chamber into the feeding means.

BRIEF DESCRIPTION OF THE DRAWINGS

The present invention will now be described in further detail by way of examples only with reference to the accompanying drawings and examples, in which

Fig. 1 is a principle drawing illustrating enteral feeding of a patient with an apparatus according to the invention,

Fig.2 is a cross-sectional principle drawing of the chamber for receiving a beneficial agent, and

Fig. 3 shows a measure of levels of beneficial agent in a feed.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Fig. 1 shows an apparatus 1 according to the invention arranged for modifying and feeding a liquid nutritional feed 6 to a patient, not shown in the drawings. The apparatus 1 comprises a chamber 3 containing a beneficial

agent. The chamber 3 is connected to a container 5 containing the nutritional feeding composition 6 via an inlet 7. An outlet 13 in the chamber 3 is connected to feeding tubes 8 and 9 which serve to lead the modified feeding composition to the patient. The feeding tube 9 extends through the nasal path and to the stomach of the patient. Pumping means is provided in the form of the chamber 3 which has a flexible wall structure 12 for pumping the liquid feeding composition 6 into the chamber 3 and back to the container 5 so as to modify the liquid feeding composition 6. In order to assure attachment between the parts 5, 7, 8, 9 and 13, conventional fastening means 17 and 18 are provided. Furthermore, a pump 10 to assist the flow from the outlet 13 and flow regulation means 11 are provided.

Fig. 2 illustrates a chamber 3 according to the invention. The chamber 3 comprises an inlet 7 and an outlet 13. A chamber wall 12 is provided in a flexible plastic, for e.g., soft Polyvinyl Chloride and a rigid lid 14 is made from a harder plastic, for e.g., hard Polyvinyl Chloride. In the present embodiment the inlet 7 is defined in the lid 14. The lid 14 may, for e.g., be sealed onto the wall 12 by ultrasonic welding or provided with threads 4 and screwed onto the wall 12.

Before use, the chamber 3 the inlet 7 and the outlet 13 are closed by thin membranes 15 and 16. For the initial mixing of a beneficial agent with a liquid feeding composition, the inlet's membrane 15 is first pierced when being connected to the container 5 shown in Fig. 1. Upon end pumping and mixing, the tube feeding 8 of Fig. 1 is to be connected to the chamber 3 which results in a piercing of the outlet's membrane 16.

EXAMPLE 1

Several liquid nutritional feeding compositions are modified and fed by

1) connecting containers of liquid, feeding to a flexible chamber according to the invention, by piercing the port in the container with the spike of the container,

2) pumping liquid from the container to the chamber and back again by squeezing and releasing the chamber 3 to 5 times, and

3) connecting the feeding means by piercing the outlet of the chamber, thus feeding the modified liquid feed composition to the feeding means. The flow is by gravity or assisted by a pump.

Tests are, for example, carried out by feeding:

1) 12 g glutamine as beneficial agent constituting about 60% of the volume of the chamber with 500 ml or 1 L liquid feed.

2) 1 g pro-biotic as beneficial agent constituting about 5% of the volume of the chamber with 500 ml or 1 L liquid feed.

3) 12 g glutamine mixed with 1 g pro-biotic as beneficial agent constituting in total about 65% of the volume of the chamber with 500 ml or 1 L liquid feed.

The liquid feeds are commercially available products such as Réabilan HN, Réabilan, Sondalis ISO, and Sondalis HP supplied by Nestlé S.A. Switzerland.

The modified feed is inspected and characterised as homogeneous.

EXAMPLE 2 - Stability

The stability of the mixture of the liquid nutritional feeding composition and the beneficial agent are controlled by the level of beneficial agent as measured by means of a calorimetric method (Kit Boehringer).

Mixtures of liquid nutritional feeding composition and beneficial agent are fed and samples are stored for 24 hours and 48 hours and the level of beneficial agent is measured.

For example, the stability of Sondalis ISO and Réabilan HN comprising Glutamine are measured over this period:

	Sondalis ISO	Réabilan HN
T= 0h	12,9 g/l	14,6 g/l
T= 24h	12.6 g/l	13,5 g/l
T= 48h	12.5 g/l	12,9 g/l

The measurements show that the Glutamine is stable above a level of 12 g/l after 48 hours.

EXAMPLE 3 - Homogenisation

The homogeneity of the modified liquid nutritional feeding composition is controlled by mixing the beneficial agent or agents with the liquid nutritional feeding composition by pumping 5 times the liquid into and out of the chamber.

The feeding tube or line is connected to the chamber and an enteral pump running at 100 ml/h, corresponding to a continuous nutrition (24h/42h).

During the feeding, after each 50 ml fed, the level of beneficial agent is measured by means of a calorimetric method (Kit Boehringer).

Fig. 3 shows the amount of beneficial agent in a feed, in the example in question the beneficial agent is Glutamine in 500 ml of 4 different liquid feeding compositions. It is apparent from the figure that the Glutamine level is homogeneous at about 12-14 g/l during the feeding period.

EXAMPLE 4

In order to verify that the geometry of the liquid containing container did not influence the homogenisation of the modified feed, trials were conducted with drip-pack, plastic pouches, and glass bottles. No difference in the homogeneity was detected from the various containers.

CLAIMS

What is claimed is:

1. An apparatus for modifying and feeding a liquid nutritional feeding composition comprising,

a chamber for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet connectable to a container containing the nutritional feeding composition and an outlet connectable to a feeding means, and

a pumping means associated with the chamber for pumping said nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition.

2. An apparatus according to claim 1, wherein the volume of the chamber being alterable for pumping of the nutritional feeding composition.

3. An apparatus according to either claim 1 or 2, wherein the chamber comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition.

4. An apparatus according to any of claims 1 to 3, wherein the chamber comprises at least one beneficial agent selected from the group consisting of nutrients, probiotics, medicaments (and diagnostic agents) or a (physiological) combination thereof.

5. An apparatus according to any of claims 1 to 4, wherein the or each beneficial agent is dispersible in the nutritional feeding composition in less than 1 min.

6. An apparatus according to any of claims 1 to 4, wherein the or each beneficial agent is dispersible in the nutritional feeding composition in less than 30 sec.

7. An apparatus according to any of claims 4 to 6, wherein the volume of beneficial agent constitutes from 30% to 50% of the volume of the chamber.

8. An apparatus according to any of claims 1 to 7, wherein the inlet is provided with a hollow spike for piercing of a port of the container and creating a fluid path for the nutritional feeding composition.

9. An apparatus according to any of claims 1 to 8, wherein the feeding means comprises a hollow spike for piercing the outlet of the chamber and creating a fluid path for the nutritional feeding composition with the beneficial agent.

10. Use of an apparatus according to any of claims 1 to 9 for modifying and enterally supplying of liquid nutritional feeding composition.

11. Use of an apparatus according to any of claims 1 to 9 for modifying and intravenous supplying of liquid nutritional feeding composition.

12. A method for modifying and feeding a liquid nutritional feeding composition comprising,

connecting a chamber according to any of claims 1 to 2 to a container comprising a liquid nutritional feeding composition,

pumping liquid feeding composition into the chamber and liquid nutritional feeding composition and beneficial agent back to the container to mix the nutritional feeding composition,

connecting the feeding means according to either claims 1 or 9, and

allowing the modified nutritional feeding composition to flow through the chamber into the feeding means.

13. A method according to claim 12, wherein the flow from the container to and through the feeding tube means, is due to gravity.

14. A method according to claim 12, wherein the flow from the container to and through the feeding tube means, is assisted by a pump.

ABSTRACT

The present invention relates to an apparatus for modifying and feeding a liquid nutritional feeding composition. Said apparatus comprises 1) chamber (5) for receiving a beneficial agent for modifying a liquid nutritional feeding composition, the chamber having an inlet (7) connectable to a container (5) containing the nutritional feeding composition and an outlet (13) connectable to a feeding means (8,9) and a pumping means associated (3) with the chamber for pumping said nutritional feeding composition from the container into the chamber and back to the container for mixing the beneficial agent into the nutritional feeding composition before connecting the outlet (13) of said chamber to the feeding means (8,9). It is preferred that the chamber (3) comprises at least one flexible wall capable of being squeezed and released for pumping of the nutritional feeding composition. The invention also relates to a method for modifying and feeding a liquid nutritional feeding composition.

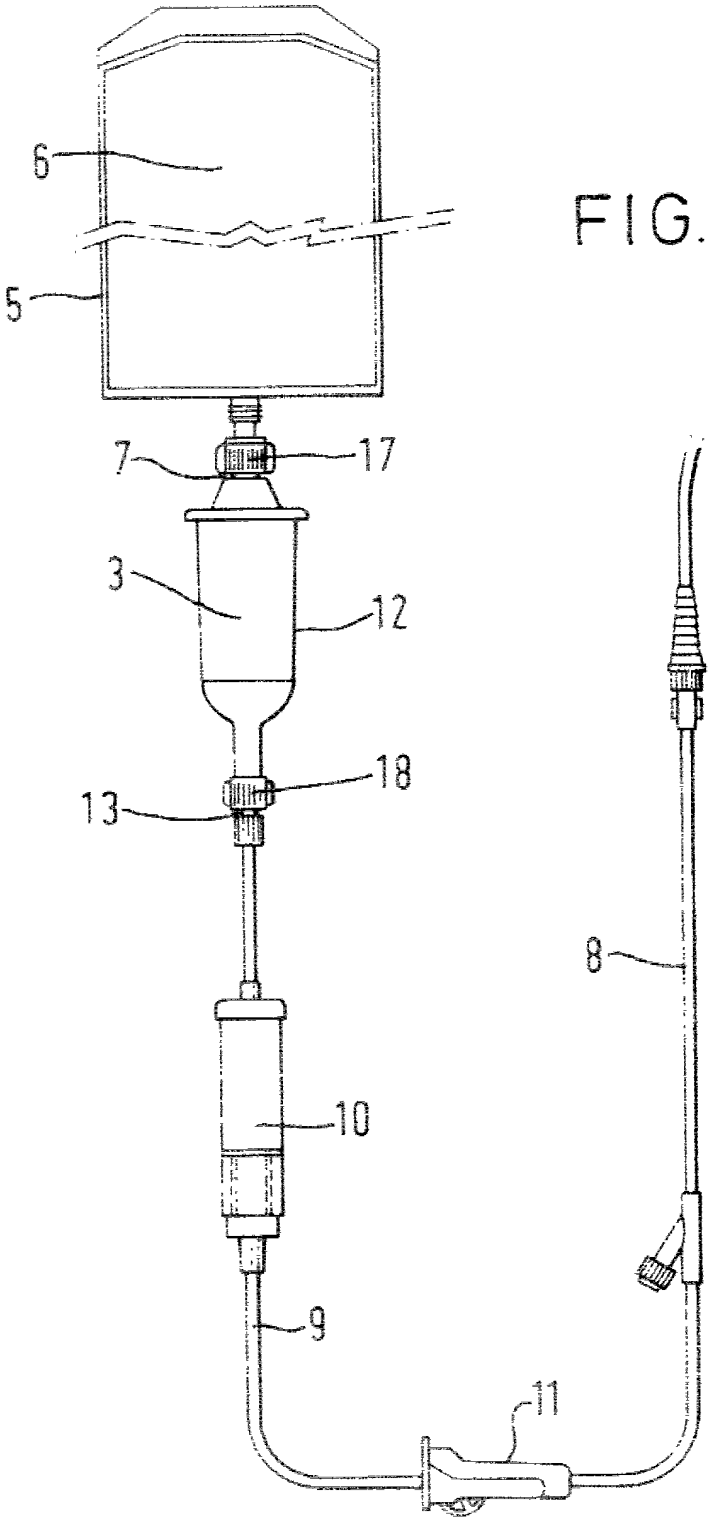


FIG.1.

FIG. 2.

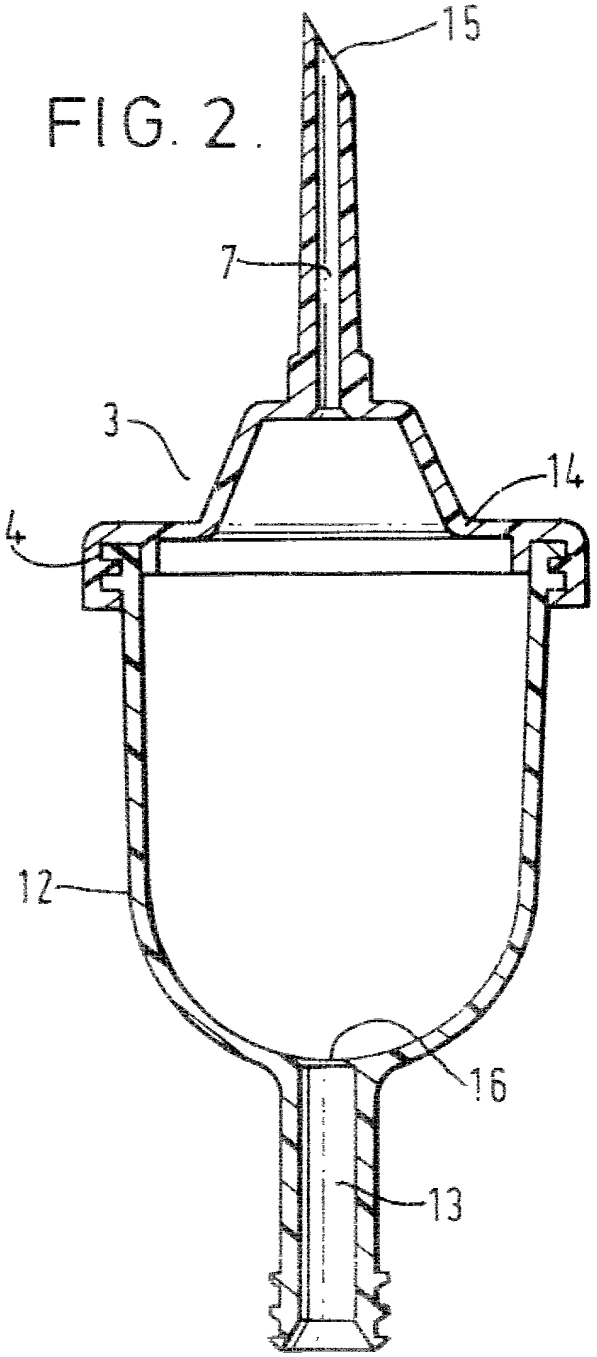
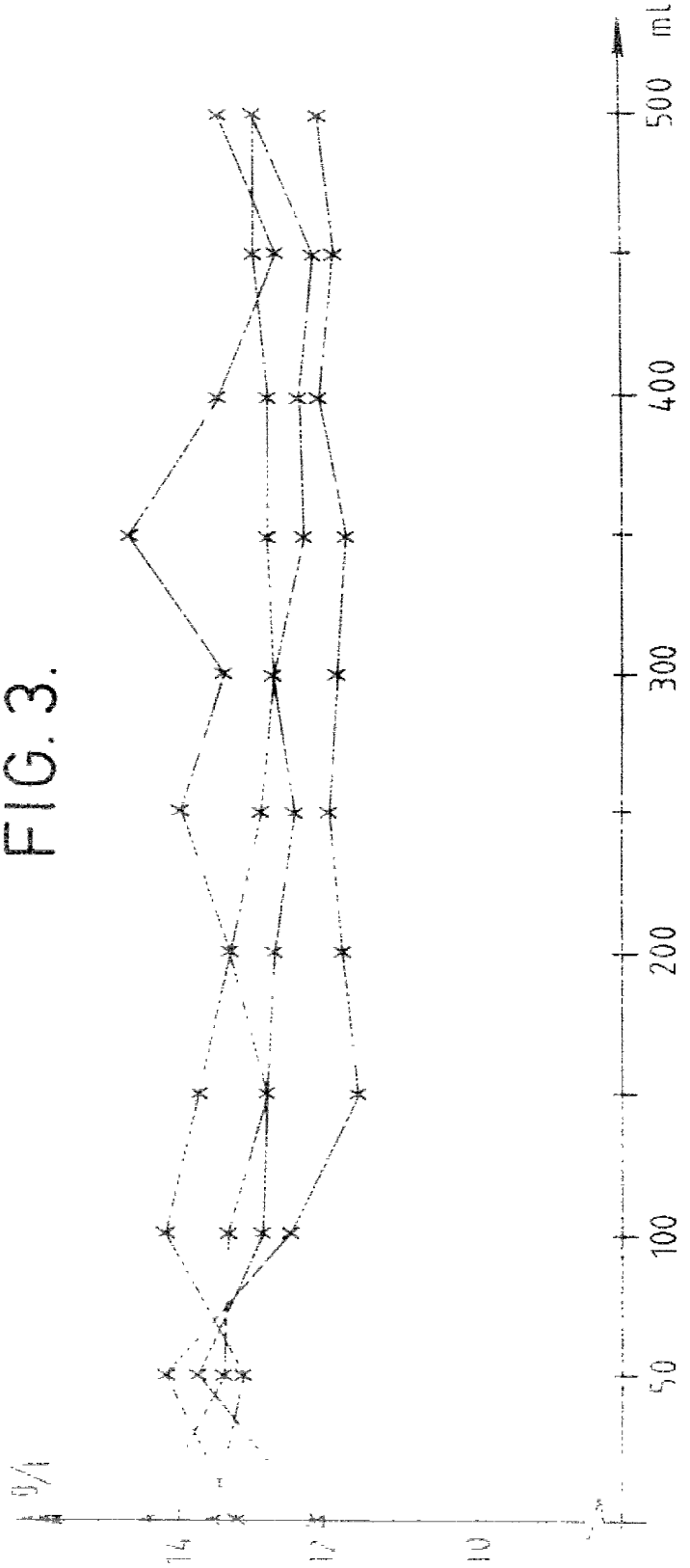


FIG. 3.



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My residence, post office address and citizenship are as stated below at 201 et seq. underneath my name.

I believe I am the original, first and sole inventor if only one name is listed at 201 below, or an original, first and joint inventor if plural names are listed at 201 et seq. below, of the subject matter which is claimed and for which a patent is sought on the invention entitled

MODIFYING AND SUPPLYING NUTRITIONAL FEEDING

and for which a patent application:

☒ is attached hereto

I hereby state that I have reviewed and understand the contents of the above identified application, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information known to me to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119(a)-(d) of any foreign application(s) for patent or inventor's certificate listed below and have also identified below any foreign application for patent or inventor's certificate having a filing date before that of the application on which priority is claimed:

EARLIEST FOREIGN APPLICATION(S), IF ANY, FILED PRIOR TO THE FILING DATE OF THE APPLICATION			
APPLICATION NUMBER	COUNTRY	DATE OF FILING (day, month, year)	PRIORITY CLAIMED
97200596.1	EPO	28/February/1997	YES ☒ NO ☐
			YES ☐ NO ☐

I hereby claim the benefit under Title 35, United States Code, §119(e) of any United States provisional application(s) listed below.

APPLICATION NUMBER	FILING DATE

I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code §112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS		
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DATE	JULY 15th 99